IN THE SPECIFICATION:

Please amend the specification as follows.

In the paragraph, on page 9, lines 3 to 8:

By the above steps (1) to (10), a DNA microarray support 100 which has avidin immobilized in a single layer to the DNA immobilizing-agent coating on ~~only to~~ the specific areas (DNA-attachable spots) 101 on the surface of the slide glass 11 is obtained. The diameter of each spot is preferably equal to or smaller than 200 mm, and the space between the neighboring spots is preferably equal to or smaller than 400 mm.

In the paragraph, on page 12, line 24- page 13, line 6:

Next, 0.1mg/ml avidin solution (Cy3-labeled streptavidin, Buffer 1xSSPE, pH7.3, Vector) was placed over the slide glass plate with the biotinylated DNA-attachable spots formed, and left at room temperature for 30 minutes. The glass plate was then washed with buffer 1xSSPE (pH7.3) for 10 minutes twice. Finally, the glass plate was washed with very-high purity water (Milli-Q water) five times and vacuum-dried. Thus a biomolecule microarray support with avidin bound to the DNA immobilizing-agent coating on the DNA-attachable spots was obtained.

IN THE ABSTRACT:

Please replace the abstract with the following.

A biomolecule microarray support prepared for immobilizing probe biomolecules to make a biomolecule microarray, including a plurality of small-sized probe biomolecule-attachable spots. The biomolecule-attachable spots are arrayed in a regular arrangement on the surface. Further, the biomolecule-attachable spots have a highly accurate uniform size and shape. The biomolecule-attachable spots are formed by covering the surface of the support other than the spots with a cover coating; subjecting the surface of the support to a biomolecule-immobilizing agent coat-forming treatment; and removing the cover coating. Alternatively, the biomolecule-attachable spots are formed by subjecting the surface of the support to a biomolecule-immobilizing agent coat-forming treatment; and covering the biomolecule-immobilizing agent coating on the surface other than the spots with a cover coating, by means of photolithography.

IN THE CLAIMS:

Please amend the claims as follows.

1. (Currently Amended) A biomolecule microarray support ~~for spotting solutions containing probe biomolecules on the surface and immobilizing the probe biomolecules in the solutions to the surface, characterized in that~~ prepared for immobilizing probe biomolecules to make a biomolecule microarray, with a plurality of small-sized ~~probe~~ biomolecule-attachable spots ~~are~~ arrayed in a regular arrangement on the surface, characterized in that the biomolecule-attachable spots have a highly-accurate uniform size and shape

formed by covering the surface of the support other than the spots with a cover coating, subjecting the surface of the support to a biomolecule-immobilizing agent coating forming treatment, and removing the cover coating, or

formed by subjecting the surface of the support to a biomolecule-immobilizing agent coating forming treatment and covering the biomolecule-immobilizing agent coating on the surface other than the spots with a cover coating,

by means of photolithography. ~~of the support.~~

2. (Currently Amended) The biomolecule microarray support of claim 1, wherein said biomolecule-immobilizing agent coating is ~~probe biomolecule-attachable spots have~~ a layer of one of probe biomolecule-immobilizing agents ~~any one of biomolecule-immobilizing agents~~ including avidin, streptavidin, biotin, amino group, carbonyl group, hydroxyl group, succinimide group, maleimide group, and thiol group.

3. (Currently Amended) The biomolecule microarray support of claim 1, wherein said support is a glass plate, silicon plate, plastic plate, gold plate, ~~or~~ gold-coated plate, ~~or~~ silver plate,

or silver-coated plate.

4. (Currently Amended) The biomolecule microarray support of claim 2 ~~claim 1~~, wherein said biomolecule-immobilizing agent coating is a layer of biotin molecules and further has a layer of avidin molecules bound to the ends of the biotin molecules. ~~probe biomolecule-attachable spots have avidin molecules bound in a single layer to the ends of the biotin molecules bound to the surface of the support.~~

5. (Currently Amended) A biomolecule microarray, characterized ~~in that probe biomolecules are bound~~ by having one of probe biomolecules DNA, RNA, PNA or protein immobilized to said probe biomolecule-attachable spots of the biomolecule microarray support of claim 1.

6. (Cancelled).

7. (Currently Amended) The biomolecule microarray of ~~claim 5~~ claim 4, wherein said probe biomolecules are biotin-labeled ~~biomolecules~~ and ~~are~~ bound to said probe biomolecule-attachable spots by biotin-avidin binding.

8. (Previously Presented) A method of fabricating the biomolecule microarray support of claim 1, comprising steps by which said probe biomolecule-attachable spots are formed only on the specific areas of the surface of a support by the photolithography and etching technique.

9. (Currently Amended) The biomolecule microarray support of claim 2, wherein said support is a glass plate, silicon plate, plastic plate, gold plate, ~~or~~ gold-coated plate, ~~or~~ silver plate, or silver-coated plate.

10. (Previously Presented) The biomolecule microarray support of claim 2, wherein said probe biomolecule-attachable spots have avidin molecules bound in a single layer to the ends of

the biotin molecules bound to the surface of the support.

11. (Previously Presented) The biomolecule microarray support of claim 3, wherein said probe biomolecule-attachable spots have avidin molecules bound in a single layer to the ends of the biotin molecules bound to the surface of the support.

12. (Previously Presented) A biomolecule microarray characterized in that probe biomolecules are bound to said probe biomolecule-attachable spots of the support of claim 2.

13. (Previously Presented) A biomolecule microarray characterized in that probe biomolecules are bound to said probe biomolecule-attachable spots of the support of claim 3.

14. (Previously Presented) A biomolecule microarray characterized in that probe biomolecules are bound to said probe biomolecule-attachable spots of the support of claim 4.

15. (Currently Amended) The biomolecule microarray of claim 5 ~~claim 6~~, wherein said probe biomolecules are biotin-labeled biomolecules and are bound to said probe biomolecule-attachable spots by biotin-avidin binding.

16. (Previously Presented) A method of fabricating the biomolecule microarray support of claim 2, comprising steps by which said probe biomolecule-attachable spots are formed only on the specific areas of the surface of a support by the photolithography and etching technique.

17. (Previously Presented) A method of fabricating the biomolecule microarray support of claim 3, comprising steps by which said probe biomolecule-attachable spots are formed only on the specific areas of the surface of a support by the photolithography and etching technique.

18. (Previously Presented) A method of fabricating the biomolecule microarray support of claim 4, comprising steps by which said probe biomolecule-attachable spots are formed

only on the specific areas of the surface of a support by the photolithography and etching technique.

19. (New) A biomolecule microarray, characterized by having one of probe biomolecules DNA, RNA, PNA, or protein immobilized to said probe biomolecule-attachable spots of the biomolecule microarray support of claim 2.

20. (New) A biomolecule microarray, characterized by having one of probe biomolecules DNA, RNA, PNA, or protein immobilized to said probe biomolecule-attachable spots of the biomolecule microarray support of claim 4.

21. (New) The biomolecule microarray support of claim 1, wherein said probe biomolecule-attachable spots are formed in the same shape as that of the pixel elements of a semiconductor imaging device used for the detection.

REMARKS

Please reconsider the application in view of the above amendments and the following remarks. Applicant thanks the Examiner for carefully considering this application.

Disposition of Claims

Claims 1-18 were pending in this application. Claim 6 has been cancelled and claims 19-21 have been added by this reply. Therefore, claims 1-5 and 7-21 are pending in this application. Claims 1-5, 7, 9, and claim 15 have been amended. The amendments are made to clarify the invention cited. No new matter has been introduced by these amendments. Claims 1, 8, 16-18, are independent. The remaining claims depend, directly or indirectly, from claims 1, 8, and 16-18.

Rejection(s) under 35 U.S.C § 112

Claim 3 was rejected under 35 U.S.C. § 112 as indefinite because the Markush group recites "or" multiple times. Claims 3 and 9 have been amended to remove the multiple "or" in the claims. Withdrawal of this rejection is respectfully requested.

Rejection(s) under 35 U.S.C § 102

A. Claims 1-7, 9-15 stand rejected under 35 U.S.C. § 102 as anticipated by Dale (U.S. Patent No. 6,440,723). Claim 6 has been cancelled in this reply. Thus, this rejection with regard to claim 6 is now moot. Claims 1-5, 7, and 9 have been amended in this reply to clarify the present invention recited. To the extent that this rejection may still apply to the amended claims, the rejection is respectfully traversed.

Two approaches are known in the prior art for the preparation of DNA microarrays: photolithography and spotting. Photolithography provides DNA detection points that are very small and uniform. In this process, the probe DNA molecules are synthesized one base at a time with the sequences determined by the mask-photo resist patterns. Thus, to synthesize an oligo probe, multiple masks and photo resists are used, which render photolithography very expensive. In contrast, the spotting method is very low cost. However, the spotting method is susceptible to variations in the volumes and concentrations of the reagents in the spotting droplets. As a result, the spotting method cannot provide small and uniform DNA detection points. Thus, DNA microarrays prepared by the spotting method often cannot be used quantitatively. Embodiments of the present invention provide improvement to the spotting method to provide detection points that are small and uniform. Embodiments of the invention have the advantages of both the spotting methods (low cost) and the photolithography method (small size, precision, and uniformity). (Specification, p. 3, line 10 – p. 4, line 17).

According to one embodiment of the invention, photolithography is used to produce specific attachment spots on a microarray support. (FIG. 1) These spots are small sized and uniform. Biotin-containing molecules are then linked to the specific attachment spots. Then, a solution containing avidin is applied to the biotin-containing molecules that have been attached to the specific spots on the support. Avidin molecules are retained by the tight avidin-biotin interactions. (FIG. 2) Note that each avidin molecule has four biotin binding sites. Therefore, the avidin molecules bound to the biotin molecules shown in FIG. 2 retain the ability to bind biotin-containing probe molecules (e.g., biotinylated probe DNA 21 in FIG. 3).

Due to the tight binding between the avidin and biotin, the binding reaction (illustrated in FIG. 2) will always reach completion. Consequently, any variation in the volumes or

concentrations of avidin used in the spotting will not affect the final concentration of the bound avidin. Therefore, embodiments of the invention can always provide uniform binding for a biotinylated probe (e.g., probe DNA 21 in FIG. 3). In addition, the attachment spots of the invention are small and uniform in size – owing to photolithography.

As amended, claim 1 recites the limitation that "the biomolecule-attachable spots have a highly-accurate uniform size and shape formed by . . . a biomolecule-immobilizing agent coating forming treatment . . . by means of photolithography."

In contrast, Dale uses a conventional spotting technique. As noted above, the conventional spotting techniques cannot provide small and uniform attachment spots. A microarray produced with the spotting technique cannot be used quantitatively. In addition, Dale discloses an array with modified oligonucleotide compositions (probe biomolecules) already associated with distinct areas on the surface of a support. In contrast, the microarray support recited in claim 1 is a general support that can be used to bind any biotinylated probe molecules to form the desired microarrays. More importantly, Dale fails to teach or suggest the limitation recited in claim 1, i.e., "the biomolecule-attachable spots have a highly-accurate uniform size and shape formed by . . . a biomolecule-immobilizing agent coating forming treatment . . . by means of photolithography."

In view of the above, claim 1 as amended is patentable over Dale. Dependent claims are allowable for at least the same reasons. Accordingly, withdrawal of this rejection is respectfully requested.

B. Claims 1-3, 5, 6, 9, 12, and 13 stand rejected under 35 U.S.C. § 102 as anticipated by Brown et al. (U.S. Patent No. 5,807,522). Claim 6 has been cancelled in this reply. Thus, this

rejection with regard to claim 6 is now moot. Claims 1-3, 5, and 9 have been amended in this reply to clarify the present invention recited. To the extent that this rejection may still apply to the amended claims, the rejection is respectfully traversed.

Brown discloses a method for forming a microarray on a solid support by tapping a capillary device that holds the solution at defined spots. (Abstract). Thus, Brown is directed to improved spotting techniques. It fails to teach or suggest the use of photolithography together with spotting. Specifically, Brown fails to teach or suggest the limitations cited in claim 1, i.e., "the biomolecule-attachable spots have a highly-accurate uniform size and shape formed by . . . a biomolecule-immobilizing agent coating forming treatment . . . by means of photolithography."

Therefore, Brown cannot anticipate claim 1 as amended. Other claims being dependent from claim 1 should be patentable for at least the same reasons. Accordingly, withdrawal of this rejection is respectfully requested.

C. Claims 1-3 and 9 stand rejected under 35 U.S.C. § 102 as anticipated by Sluka et al. (U.S. Patent No. 6,221,674). Claims 1-3 and 9 have been amended in this reply to clarify the present invention recited. To the extent that this rejection may still apply to the amended claims, the rejection is respectfully traversed.

Sluka discloses a process with which array structures of reagents spots can be applied in a simple manner to metal or metal oxide surfaces. (Col. 2, lines 5-7). The reagent spots can for example be applied by means of ink-jet methods or with an automatic micropipetting device. (Col. 2, lines 19-21). Thus, Sluka is directed to spotting techniques specific for metal or metal oxide surfaces. It fails to teach or suggest the use of photolithography together with spotting. Specifically, Sluka fails to teach or suggest the limitations cited in claim 1, i.e., "the

biomolecule-attachable spots have a highly-accurate uniform size and shape formed by . . . a biomolecule-immobilizing agent coating forming treatment . . . by means of photolithography."

Therefore, Sluka cannot anticipate claim 1 as amended. Other claims being dependent from claim 1 should be patentable for at least the same reasons. Accordingly, withdrawal of this rejection is respectfully requested.

Conclusion

Applicant believes this reply to be fully responsive to all outstanding issues and place this application in condition for allowance. If this belief is incorrect, or other issues arise, do not hesitate to contact the undersigned or his associates at the telephone number listed below. Please apply any charges not covered, or any credits, to Deposit Account 50-0591 (Reference Number 05426.014001).

Respectfully submitted,

Date: 10/14/03

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